

(19) Japanese Patent Office (JP)

(11) Patent Application Publication Number

S 64-4012

(12) Published Patent Application (A)(51) Int. CL.⁺ Identification JPO File (43) Publication Date: 10 February 1989

Code Number

A 61K 7/00 H-7306-4C

7/48 G-7306-4C

6971-4C

Request for Examination: No, Number of

Invention: 1 (5 pages)

(54) Title of the Invention Cosmetic

(21) Application Number: S62-196928

(22) Filing Date: 6 August 1987

(72) Inventor Kamisaka Hiroshi Room #1 Takashimaya Street # 27, Kanagawa-ku, Yokohama-shi, Kanagawa, Japan
Within the Yokohama Research Institute of POLA Chemical Industries, Inc.

(72) Inventor Shaku Masao Room #1 Takashimaya Street # 27, Kanagawa-ku, Yokohama-shi, Kanagawa, Japan
Within the Yokohama Research Institute of POLA Chemical Industries, Inc.

(71) Applicant POLA Chemical Industries, Inc. 648 Yayoi-cho, Shizuoka-shi, Shizuoka, Japan

Specification

1. Title of the Invention

Cosmetic

2. Claims

5 A cosmetic characterized by blending vitamin A with estrogen.

3. Detailed Description of the Invention

10 (Field of the Invention)
The present invention relates to a cosmetic capable of remarkably improving the softness, resiliency and surface condition of skin. More specifically, the present invention provides a cosmetic characterized by blending vitamin A with estrogen as active ingredients. The cosmetic of the present invention is capable of providing hydration to the skin, improving physiological functions of the skin and remarkably improving softness, resiliency and surface condition of the skin.

(Prior Art)

25 As skin ages, its water retention ability decreases, resulting in dry, rough and coarse skin texture without moisture. This is caused by reduced glycosaminoglycans in the skin with aging.

30 The prior cosmetics were compounds with insufficient glycosaminoglycans in the

skin, wherein the hyaluronic acid with strong ability of water retention was capable of providing appropriate hydration to the skin to make it smooth (Japanese Patent Publication No. S 33-500 and Japanese Patent Publication No. S 55-160712). However, due to limited effects of supplementing moisture-retention ingredients from outside the skin, the formulation contains physiologically active substance related to synthesis of hyaluronic acid, thereby enhancing the internal working function and humectant properties of the skin. For example, there are a cosmetic containing estrogen capable of enhancing biosynthesis of dermic hyaluronic acid and a cosmetic for synergistic effects by combining estrogen and glycosaminoglycan (a technique as disclosed in Japanese Published Unexamined Application No. S53-25311), and a cosmetic containing vitamin A or a combination of glycosaminoglycan and vitamin A to enhance the biosynthesis of epidermal hyaluronic acid (a technique as disclosed in Japanese Published Unexamined Application No. S60-252405).

(Problems to be Solved by the Invention)

The long-term recovery effect is not adequate in the cosmetic blended with glycosaminoglycan only because the glycosaminoglycan supplemented from outside the skin can be easily washed away by face washing and sweating. A long-term effect can be expected from estrogen and vitamin A that work on the inside of the skin, but of most products with the estrogen effects on dermis, a cosmetic blended with glycosaminoglycan is closely related to the epidermal state and has little effect on delivering appropriate hydration to the skin surface, and of most products with the vitamin A effects on epidermis, a cosmetic blended with vitamin A and glycosaminoglycan is believed to have little effect on dermis controlling resiliency and appropriate tension of the skin. Therefore, the prior techniques are not adequate in enhancing the moisture retention of all skin tissues, and do not show to have sufficient effects on softness, resiliency and humectant properties of the skin.

(Means for Solving the Problems in the Invention)

The inventors of the present invention have focused on studying a cosmetic blended with estrogen that makes the skin resilient and elastic by increasing the biosynthesis of glycosaminoglycan in the epidermis, and enhancing the biosynthesis of vitamin A and dermal glycosaminoglycan that helps to smooth and appropriately hydrate the skin, and the present invention was completed with the findings that the skin softness, resiliency and surface condition were remarkably improved by blending with vitamin A, estrogen or glycosaminoglycan alone, the combination of estrogen and glycosaminoglycan, as well as the combination of vitamin A and glycosaminoglycan.

Accordingly, the present invention provides a cosmetic obtained by blending the combination of vitamin A and estrogen, capable of enhancing biosynthesis of glycosaminoglycan of the entire skin including epidermis and dermis, and keeping the skin in balance, thereby providing hydration to the skin, enhancing the softness and humectant properties of the

skin and helping to prevent skin aging, such as feel of dryness.

The invention is explained in details below.

The estrogen of the invention is optionally selected from one or more among, for example, retinol, retinal, 17- β -estradiol, estrone, estriol, diethylstilbestrol, hexestrol and etc.. The blending amount is between 0.0001 weight% and 0.05 weight% (the amount less than 0.0001% will have no effect and that more than 0.05% will have a risk of side effects, and the range between 0.001 and 0.01% is preferred).

The vitamin A of the invention is optionally selected from one or more of, for example, retinol, retinal, dehydroretinol, dehydroretinal and esters thereof, or provitamins such as carotene, lycopene, zeaxanthin, cryptoxanthin, echinenone and etc.. The blending amount of vitamin A is between 0.0001 weight% and 0.05 weight% (an amount of less than 0.0001% will have no effect and that of more than 0.05% will have a risk of side effects, and the preferred range is from 0.001 to 0.01%).

In addition, the ratio of estrogen and vitamin A that is effective for skin is preferably in the range of 1:1/2-2.

In addition to these ingredients, the cosmetic of the present invention can also be formulated with various essential ingredients generally used in cosmetic and pharmaceutical products, for example, aqueous ingredient, powder ingredient, oil, surfactant, humectant, thickener, antioxidant, flavor, coloring materials, ultraviolet ray absorber, vitamins, pharmaceutical agents and etc., at a range not impairing the effectiveness of the present invention. Also, different from the composition ratio of vitamin A and estrogen stated above, the glycosaminoglycan is blended in the range between 0.01% and 10% to supplement the cosmetic produce with the effects of vitamin A and estrogen (the blending ratio of less than 0.01% is not sufficient to deliver the effect, but that of more than 10% is undesirable).

Furthermore, glycosaminoglycans used herein are, for example, hyaluronic acid, chondroitin sulfate A, chondroitin sulfate B, chondroitin sulfate C, etc., and/or salts

thereof. The bases forming the salt of glycosaminoglycan can be inorganic salts such as lithium hydroxide, potassium hydroxide, etc., organic salts such as 10 triethanolamine, etc., and base amino acids such as lysine, arginine, β -amino, etc.

The present invention and its effects are described using the following embodiments.

(The space below is intentionally left blank)

Ingredient	Embodiment 1	Control Example 1	Control Example 2	Control Example 3
Stearic acid	10.0	"	"	"
Stearyl alcohol	5.0	"	"	"
Stearic acid butyl	8.0	"	"	"
Stearic acid monoglycerin ester	3.0	"	"	"
Retinyl estradiol	0.004	0.004	—	—
Retinol	0.004	—	0.004	—
Flavor	Appropriate amount	"	"	"
Propylene glycol	5.0	"	"	"
Glycerin	8.0	"	"	"
Ion exchange water	Residual	"	"	"

(Manufacturing method)

Ingredient A (oil phase) and ingredient B (aqueous phase) were completely dissolved respectively by heating to 70 °C, and then the oil phase was mixed and emulsified in aqueous phase, and the manufacturing was completed when it had been cooled to 30 °C with a heat exchanger. (Tests used)

Tests were used to evaluate the effects of the cosmetic of the present invention. Forty woman panelists were divided into 4 groups with 10 in each group. Group 1 received the cream of Embodiment 1, Group

2 received the cream of Control Example 1, Group 3 received the cream of Control Example 2 and Group 4 received the cream of Control Example 3. The creams were all tropically applied, once daily for 20 days. After 20 days, the effectiveness was determined based on the two indexes, "resiliency and elasticity of skin" and "moisturized feel of skin". Results are shown in Table 1.

(The space below is intentionally left blank)

Table 1

Evaluation items	Embodiment 1	Control Example 1	Control Example 2	Control Example 3
Resiliency and elasticity of skin	9/10 ***	6/10 ss	3/10 ss	0/10 ***
Moisturized feel of skin	8/10 ***	2/10 ss	6/10 **	0/10 ***

a) Number of subjects/members believed to have response

*** There is a significant difference for Control Example 3 as the risk ratio $P < 0.001$

** There is a significant difference for Control Example 3 as the risk ratio $P < 0.01$

(tested with X^2)

ss There is a significant difference for Embodiment 1 as the risk ratio $P < 0.001$ ss. There is a significant difference for Embodiment 1 as the risk ratio $P < 0.01$

Formulation 2 Lotion

Ingredient	Embodiment 2	Control Example 4	Control Example 5	Control Example 6
Ethanol	5.0	"	"	"
POE oleyl alcohol ether	2.0	"	"	"
Retinyl estradiol	0.003	0.003	—	—
Retinol	0.003	—	0.003	—
Flavor	Appropriate amount	"	"	"
1,3-butylene glycol	10.0	"	"	"

B

Glycerin	5.0	"	"	"
Purified water	Residual	"	"	"
Sodium hyaluronate	—	0.2	0.2	—

(Manufacturing method)

Ingredient A (oil phase) is added to 1.5
ingredient B (aqueous phase), and is
5 uniformly emulsified by a homomixer at the
temperature of 70 °C and is then cooled.

(Tests used)

Forty panelists spontaneously reporting 20
their symptoms of skin were divided into
10 four groups. Group 1 received the product
of Embodiment 2, Group 2 received the
product of Control Example 4, Group 3

received the product of Control Example 5
and Group 4 received the product of Control
Example 6. The products were all tropically
applied for a month. The effectiveness was
determined based on whether the rough skin
was improved. Results are shown in Table
2.

(The space below intentionally left
blank)

Table 2

	Embodiment 2	Control Example 4	Control Example 5	Control Example 6
Number of subjects with improvements in the rough skin	9/10***	4/10*s	4/10*s	0/10***
Number of panels				

*** There is a significant difference for
Control Example 6 as the risk ratio $P < 0.001$

* There is a significant difference for
Control Example 6 as the risk ratio $P < 0.05$ 40
(tested with χ^2)

sss There is a significant difference for
Embodiment 2 as the risk ratio $P < 0.001$

s. There is a significant difference for
Embodiment 2 as the risk ratio $P < 0.05$ 45
(tested with χ^2)

These results showed a cosmetic
formulated with vitamin A and estrogen is
confirmed to have the effects of "improving
rough skin", remarkably enhancing the
"resiliency" and "moisturized feel" of skin
by using vitamin A or estrogen alone or
combination of vitamin A and
glycosaminoglycan, or combination of
estrogen and glycosaminoglycan.

The examples of formulations are
further described as follows.

Formulation 3 Foundation

Hydrophobic titanium oxide microparticles	7.0
Isostearic acid triglyceride	2.0
2-octyldodecyl neopentanoate	8.0
Liquid paraffin	3.0
Cetyl alcohol	5.0
Candelilla wax	2.0
POE (25) monostearate	2.0
Sorbitan monostearate	1.0
Yellow iron oxide	1.3
Colcochar	0.8
Polyethylene glycol	4.0
Methylparaben	0.2
Sodium hyaluronate	0.5
Flavor	0.2
Diethylstilbestrol	0.002
Retinal	0.002
Purified water	Residual

Embodiment 4 Back

Polyvinyl alcohol	20.0
Ethanol	20.0
Sodium hyaluronate	0.2

Glycerin	5.0
Flavor	0.3
Ethinyl estradiol	0.004
Retinal	0.004
Purified water	Residual
Embodiment 5 Oil	
Squalane	47.0
Castor oil	47.0
Diethylstilbestrol	0.005
Retinal	0.005
Purified water	Residual

Patent Applicant	POLA
Chemical Industries, Inc.	

[Publication Classification] Revision published pursuant to provisions under Article 17(2) of the Patent Law	
[Department/Section] Section 2 of Department 3	
[Issuing Date] 14 March 1995	
[Publication Number] H1-0412	
[Publication Date] 10 February 1989	
[Annual Serial Number] Public Official Gazette 1-405	
[Application Number] S62-196928	
[International Patent Classification - 6 th Edition]	
A61K 7/00 H9051-4C	
7/48 G 9051-4C	
9053-4C	
Amendments 1 August 1994 To Director General of Patent Office,	"Detailed Description of the Invention" in the Specification as follows.
1. Indication of the Case Patient No. 196923 of 1987 (2) Title of the Invention Skin cosmetic 3. Person Making the Revision Relationship with the case Patent	1) The word "cosmetic" mentioned in line 1 on page 3 in the Specification is revised as "skin cosmetic". 2) The word "cosmetic" mentioned in line 1 on page 10 in the Specification is revised as "skin cosmetic". 3) The "vitamin A... cosmetic" mentioned in lines 11-13 on page 11 in the Specification is removed. 4) The "that" mentioned in line 18 on page 1 in the Specification is revised as "that related to skin cosmetic". 5) The word "cosmetic" mentioned in line 5 from the bottom on page 4, line 1 on page 6, line 7 on page 9 and line 2 on page 14 in the Specification is revised as "skin cosmetic". 6) The word "formulation example" mentioned in line 9 on page 14 in the Specification is revised as "embodiment". 7) The word "formulation" mentioned in line 10 on page 14 in the Specification is revised as "embodiment".
Applicant 6-48 Yayoi-cho, Shizuoka-shi, Shizuoka, Japan POLA Chemical Industries, Inc. 4. Agent Postal Code 107 1-9-15, Akasaka, Minato-ku, Tokyo, Japan Nippon Short-Wave Broadcasting House Tel.: 03 (3583) 7058 (7849) Attorney Toshiro Mitsuishi The same domicile as above (7448) Attorney Tadataka Mitsuishi	60 60 70 75
5. Date of Notifying the Reason for Rejection	80
Spontaneously 6. Item for Revision The sections of "Claims", "Title of the Invention" and "Detailed Description of the Invention" in the Specification	85
7. Contents for Revision (1) Revisions have been made on a separate sheet for the section of "Claims" in the Specification.	90
(2) Revisions have been made for the sections of "Title of the Invention" and - Appendix 1 -	8. Table of Contents of Attached Documents (1) Revised Claims 1 End

Revised Claims

A skin cosmetic characterized by blending vitamin A with estrogen.